

SUPPLEMENTAL AMENDMENT UNDER 37 C.F.R. § 1.111
Attorney Docket No.: Q76104
U.S. Application No.: 10/611,902

REMARKS

The present invention relates to a method for treating a tumor comprising the step of administering a composition containing benzyl alcohol (also sometimes referred to herein as BA).

In the Amendment filed April 3, 2006, claims 1, 2, 4 - 7 and 16 - 17 were amended; claim 5 was canceled. However, it has been found, upon a confirmation review of the Amendment, that claims 4, 6, and 7 were not amended as intended. Particularly in claims 4, 6, and 7, Applicants had intended that the other ingredient to be used in combination with the benzyl alcohol was to have been limited to vitamin C, but inadvertently the recitation of "vitamin C" was instead deleted.

Therefore, in this Supplemental Amendment, claims 4, 6, and 7 have been amended to specify that the ingredient used in combination with the benzyl alcohol is vitamin C, and not heparin. Furthermore, claim 4 has been placed in the form of an independent claim, and hence has been further amended consistent with the amendments made to claim 1 in the Amendment filed April 3, 2006. Lastly, claims 16 and 17 are further amended herein to depend on claims 1 - 4, 6, and 7 since claim 5 was canceled in the Amendment filed April 3, 2006.

The amendments to the claims herein are supported by the recitations of the original claims, etc.

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Below, Applicants further explain the patentability of the claims as amended herein vis-à-vis the rejections that were set forth in the Office Action of October 3, 2005. The explanation is essentially similar with respect to the rejections under 35 U.S.C. § 102, is consistent with the present amendments to claims 4, 6, and 7 with respect to the rejections under 35 U.S.C. § 103, is pertinent in relation to the evidentiary showing of the Declaration Under 37 C.F.R. § 1.132 (copy attached), as well as with respect to the rejection under 35 U.S.C. § 112, first paragraph.

Response to Claim Rejections Under 35 U.S.C. § 102

A. Bessette (WO 00/33857)

At page 2 of the Office Action, claims 1-3, 5, 8, and 9 were rejected under 35 U.S.C. § 102(b) as being anticipated by Bessette (WO 00/33,857).

Specifically, it was asserted that Bessette teaches a pharmaceutical composition for the treatment of soft tissue cancer in mammals comprising at least one plant essential oil. It was also stated that the reference includes a specific embodiment where the plant oil is benzyl alcohol. In addition, it was stated that the reference specifically teaches treatment of human breast cancer cells (MCF-7) with 50 µg/ml benzyl alcohol.

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sufficient to cause cells of the tumor to become necrotic. In contrast, the experimental results described in Bessette indicate that benzyl alcohol's (BA's) antitumor effect on breast cancer cells is caused by "protection against the E2-induced abnormal growth in cancer breast cells." The experimental system used in Bessette does not use the death rate of cancer cells as a marker. Further, Bessette does not teach or suggest that BA administration causes tumor cells to become necrotic.

In fact, Fig. 1 of the Certified Experimental Result 1, shown in the Declaration of Dr. Takeyama submitted herewith, demonstrates that BA administrated at the concentration described in Bessette does not cause changes in adhesive property or cell death. Specifically, BA was administrated at a concentration of 50µg/ml, as described in Example 3 of Bessette. The results in the Declaration show that administration at a concentration of 50µg/ml does not cause tumor cells to become necrotic. Therefore, Bessette does not teach or suggest that BA administration at the concentration recited in the present claims induces necrosis in cancer cells.

In view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection.

B. References PP-1457 and B-323

At pages 3 and 4 of the Office Action, claims 1-3, 5, 8, and 9 were rejected under 35 U.S.C. § 102(b) as being anticipated by "The antitumor effect to stomach cancer by benzyl

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alcohol,” Meeting of Japan Surgical Society on April 12-14, 2000, issued on March 10, 2000, PP-1457, hereafter referred to as “Reference PP-1457;” and by “The antitumor effect of benzyl alcohol against breast cancer,” The 10th Annual Meeting of the Japanese Breast Cancer Society, July 5-6, 2002, B-323, hereafter referred to as “Reference B-323.”

According to the Office Action, the references teach that benzyl alcohol induces apoptosis in stomach cancer cells (PP-1457) and breast cancer cells (B-323).

Both PP-1457 and B-323 disclose that administration of BA at concentrations of 300µg-1000µg has an antitumor effect on stomach cancer or breast cancer. However, administration of BA at concentrations of 300µg-1000µg is not sufficient to induce tumor cell death (see Fig. 1 in the enclosed Declaration).

In addition, PP-1457 discloses that death of stomach cancer cells is caused by apoptosis rather than necrosis. Similarly, B-323 discloses that death of MCF-7 (a breast cancer cell line) cells is caused by apoptosis rather than necrosis, and that the reason for BSMZ (another breast cancer cell line) cell death is not known.

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Response to Claim Rejections Under 35 U.S.C. § 103

At page 5 of the Office Action, claims 1-17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Smorenburg, et al. (2001) Pharmacological Reviews, 53(1):93-105 (Smorenburg), in view of Bessette, and in light of Stedman's Medical Dictionary, 25th Edition (1990), 1026-1027.

Specifically, it was contended that Smorenberg teaches heparins as anti-cancer drugs. Bessette was cited for the description of benzyl alcohol (BA). Considering both references, the Office Action suggested that it would have been obvious to a person having ordinary skill in the art to combine heparin and BA simply based on asserted showing of the prior art that each compound alone has been used for treating cancerous tumors.

In response, first, Applicants must again reemphasize that the present inventors have discovered that administration of BA at an appropriate concentration causes tumor cells to become necrotic. The cited references do not teach or suggest tumor cell death by necrosis, nor the appropriate concentration of BA to administer to cause tumor cell death by necrosis. Therefore, a person of ordinary skill in the art would not have been able to predict the method recited in the present claims based on the cited Smorenberg and Bessette references in light of Stedman's Medical Dictionary.

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Furthermore, with respect to the Smorenberg teaching of using heparin as an anticancer drugs, it is noted that claims 4, 6, and 7 have been amended herein and do not recite heparin. Rather, amended claims 4, 6, and 7 recite combination therapy using BA together with vitamin C.

There is no combination of teachings in the cited references of record that would lead to the combination therapy of using BA together with vitamin C in accordance with amended claims 4, 6, and 7. Still further, the Examiner's attention is directed to the experimental result set forth in Certified Experimental Result 2 under 37 C.F.R. § 1.132. The experiment shows the combined administration of BA with vitamin C can cause an antitumor effect even at very low concentration (BA: 39.1 µg/ml, vitamin C: 391 µg/ml, referring to page 4 of the § 1.132 Declaration) compared to the administration of BA alone.

There is no basis whatsoever in the prior art by which a person of ordinary skill in the art would have expected such a result.

For all of the above reasons, Applicants respectfully submit that the rejection under 35 U.S.C. § 103 should be withdrawn.

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Response to Claim Rejections Under 35 U.S.C. § 112 First Paragraph

In the Office Action, at page 7, the claims were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being fully enabling with respect to the previous scope of the claims, with the Examiner indicating that the specification did enable a method of treating stomach tumor cells, breast tumor cells, large bowel tumor cells, thyroid gland tumor cells, and pancreatic tumor cells with benzyl alcohol. Accordingly, claim 1 was amended as noted above, and claim 4 has been amended analogously in view of the amended recitation of claim 4 to present claim 4 as an independent claim. Furthermore, it has been noted above, Experimental Result 2 of the Declaration under 37 C.F.R. § 1.132 further illustrates the benefit of the combination therapy using BA and vitamin C.

Accordingly, it is respectfully submitted that the rejection under 35 U.S.C. § 112, first paragraph has been overcome, and should now be withdrawn.

Conclusion

The Examiner now is respectfully requested to proceed with examination of the claims as amended herein further responsive to the issues that have been raised, and to withdraw the remaining rejections and allow claims 1 - 4, 6 - 7, and 16 - 17.

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In view of the above, reconsideration and allowance of the pending claims of this application are now believed to be in order, and such actions are hereby earnestly solicited.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at attorney at the local Washington, D.C. telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

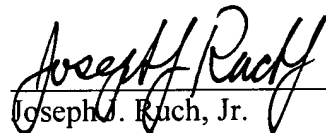
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